The University of Michigan
Acute Care Surgery

ARDS: Risk Factors, Prognostic Factors, Management and Outcomes

TABLE OF CONTENTS

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
03 SEP 2009	**Final**	**10-09-2007 to 03-09-2009**

4. TITLE AND SUBTITLE
ARDS: Risk Factors, Prognostic Factors, Management and Outcomes Incidence and Mortality of ARDS in Combat Casualty Care

5a. CONTRACT NUMBER
FA 70 14-07-C-AOIO

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER
Log 99, BAA 07-01

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
University of Michigan Health Systcm,University I-lospital,1500 East Medical Center Drive,Ann Arbor,MI,48109-0033

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Air Force Surgeon General's Office, Modernization Research and Development Division, 5201 Leesburg Pike, Falls Church, VA, 22041-3268

10. SPONSOR/MONITOR'S ACRONYM(S)
AFMSA/SGR

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The incidence and mortality of Acute Respiratory Distress Syndrome (ARDS) and utilization of resources for ARDS treatment in current combat casualty care was investigated through a query of the Joint Theater Trauma Registry. Development of ARDS was found to be significantly associated (p =.05) with higher military injury severity scale (ISS), low admission systolic blood pressure (SBP), and female gender. Blast injury was the most common mechanism of injury in ARDS patients but was not confirmed as an independent risk factor for ARDS development. Mortality among ARDS patients was independently associated with higher ISS, low SBP and lower Glasgow Coma Scale and was significantly increased in intubated patients when ARDS was present. Critical care resource utilization was significantly greater for ARDS patients. ARDS still accounts for death in 0.4% of hospitalized casualties in current military medical care. Further investigations of ARDS prevention and evaluation of resuscitation strategies as a risk factor is warranted. Long-term follow up of ARDS survivors in combat casualty is necessary.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**1**	**54**	

The University of Michigan
Acute Care Surgery

ARDS: Risk Factors, Prognostic Factors, Management and Outcomes

INTRODUCTION

July, 2009

Introduction

Acute respiratory distress syndrome (ARDS) is the sudden, often fatal, acute process by which there is moderate to severe loss of lung function. This occurs following another acute medical condition, such as trauma, pneumonia, sepsis and other etiologies. Each year in the United States there are more than 200,000 cases of acute lung injury (ALI) and ARDS, which are associated with over 75,000 deaths and over 4 million intensive care unit and hospital days of care. The mortality and morbidity rates associated with ALI and ARDS are considerable, with significant impact on public health. The in-hospital mortality rate is very high, with reports ranging from 38.5% to greater than 50%. Most patients who survive ARDS and do not have pre-existing lung disease regain excellent lung function. The challenge is getting them to survive ARDS and its associated severe hypoxemia.

Of particular concern are the reports of combat casualties with severe ARDS in young, otherwise healthy, injured military personnel, some relating to bomb blasts. Setting up systems to provide optimal ALI and ARDS care and management within the Department of Defense, particularly in the far-forward arena and in combat support hospitals, is particularly important to both maintain readiness and force protection, as well as in the continued provision of clinical care during transport and in the provision of definitive care. Research investigation regarding risk factors for ALI and ARDS in the combat setting is also of great importance, since potential efforts to prevent ARDS could be undertaken if these factors are identified. Support of this ARDS research is critical in meeting the needs of military combat casualties. Tested ARDS prevention, prognostic and treatment strategies developed by University of Michigan could ultimately reduce death related to ALI and ARDS, and potentially prevent ALI and ARDS as a complication in injured military personnel.

This Joint Theater Trauma Registry (JTTR) data query seeks to assess the epidemiology and specific risk factors for ARDS in military combat casualties and review current ARDS treatment strategies and outcomes. Specific risk factors that will be investigated include blood transfusion, bomb blast injury, altitude, and patient outcome (survival vs. ALI/ARDS-related death vs. death unrelated to ALI/ARDS).

HYPOTHESES/RESEARCHQUESTIONS:

- What is the epidemiology of ALI/ARDS in combat casualty care in injured military personnel?
- What are the specific risk factors for ALI/ARDS in combat casualty care?
- Is blood transfusion a specific risk factor for ALI/ARDS in combat casualty care?
- Is bomb blast injury or altitude a specific risk factor for ALI/ARDS in combat casualty care?
- What are the current ARDS treatment strategies that are being used in combat casualty care?
- What are the short-term outcomes (ICU & hospital mortality, ICU & hospital length of stay, duration of ventilation, ventilator-free days, organ failure) of patients with ALI/ARDS in combat casualty care?

Incidence and Mortality of ARDS in Combat Casualty Care

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Running Head: ALI and ARDS in Combat Casualty

Key Words: Acute lung injury, acute respiratory distress syndrome, respiratory failure, hypoxemia, hypercarbia, mortality, outcome

Presented, in part, at the American Association for the Surgery of Trauma 66th Annual Meeting
September 27-29, 2007, Las Vegas, Nevada

Grant Funding: "ALI/ARDS: Risk Factors, Prognostic Factors, Management and Outcome"
Contract Number FA7014-07-C-A010, Log 99, BAA 07-01
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Abstract

Objective: Advances in military medicine and transport have improved coordinated trauma care delivery to the critically injured soldier. In the Vietnam War, approximately 0.4% of hospitalized casualties died from ARDS. We sought to evaluate the current incidence, mortality and resource utilization of ARDS in current combat casualty care.

Methods: The Joint Theater Trauma Registry was queried for US military personnel (excluding non-US, non-military cases) injured between June 8, 2001 and July 17, 2008. The cohort was classified as having 1) ARDS, 2) intubation, without ARDS, or 3) neither. Demographics, trauma variables & outcomes were compared.

Results: The query yielded 4666 individuals with 4700 separate records. 152 ARDS cases (3.2%) were identified; overall mortality was 12.6%. ARDS was associated with female gender (5.2 vs. 2.2%, $p<0.05$) and with higher ISS (ISS $\geq$ 25 in 36.8% of ARDS patients vs. 27.0% in non-ARDS intubated group and 2.6% in non-intubated cohort, $p<0.05$), shock and tachycardia at the first point of medical care. Ventilator days, ICU days and LOS were significantly increased in the ARDS group.

Variable	ARDS	Non-ARDS Intubated	Neither	All
N	152	2213	2335	4700
Age, mean ± SD	26.1 ± 6.0	25.8 ± 6.5	26.4 ± 6.8	26.1 ± 6.6
Gender F, % (n)	5.2 (8) *§	2.2 (47) §	2.6 (63)	2.6 (118)
Blast Injury, % (n)	69.8 (106) §	70.0 (1550) §	58.6 (1370)	64.4 (3026)
GCS 3-8, % (n)	42.6 (60) §	44.8 (907) §	2.4 (40)	25.8 (1007)
ISS05 ≥ 25, % (n)	36.8 (56) *§	27.0 (597) §	2.6 (61)	15.2 (714)
BP ≤ 90 on admit, % (n)	14.6 (22) *§	8.8 (186) §	2.0 (43)	5.6 (251)
HR≥ 90 on admit, % (n)	69.6 (105) *§	61.0 (1306) §	35.6 (806)	48.6 (2217)
Vent days, mean ± SD	7.1 ± 5.7 #	3.7 ± 3.6 #	1.0 ± .2	2.5 ±3.1
ICU days, mean ± SD	11.2 ± 10.1 #	5.6 ± 7.0 #	1.5 ± 1.3	3.7 ± 5.7
LOS, median (range)	11.0 (0-142) #	5.0 (0-1171) #	5.0 (0, 737)	5 (0-1171)
Mortality, % (n)	12.6 (19) §	8.8 (193) §	3.2 (75)	6.2 (287)

*$p < .05$ compared to Non-ARDS, intubated, § $p < 0.05$ compared to Neither by X^2 statistic
#$p < 0.001$ compared to Non-ARDS, intubated by Wilcoxon scores test

Conclusions: ARDS remains a significant complication in current combat casualty care, and is associated with female gender, higher injury severity and adverse outcomes. ARDS still accounts for death in 0.4% of hospitalized casualties in current military medical care.

Introduction:

Acute respiratory distress syndrome (ARDS) is the sudden, often fatal, acute process by which there is moderate to severe hypoxemia and respiratory failure. The syndrome was first described by surgeons in Vietnam as a complication of severe injury and the need for aggressive fluid resuscitation for traumatic shock (DaNang Lung). [1] From this first description, further investigations have refined the description of the constellation of clinical criteria consisting of acute hypoxemic respiratory failure with bilateral radiographic opacities that may coexist with, but is not fully explained by, hydrostatic pulmonary edema. [2] The North American-European Consensus Conference Committee broadened the definition to include patients with milder hypoxemia (termed Acute Lung Injury, ALI criteria: PaO_2/FiO_2 <300 mm Hg, bilateral infiltrates on CXR, no left atrial hypertension) and defined the more severe hypoxemia as ARDS (ARDS criteria: PaO_2/FiO_2 <200 mm Hg, bilateral infiltrates on CXR, no left atrial hypertension). [3]

The mortality and morbidity rates associated with ALI and ARDS are considerable, with significant impact on public health worldwide. Each year, in the U.S. alone, there are more than 150,000 cases of ALI and ARDS, which are associated with over 75,000 deaths and over 4 million intensive care unit and hospital days of care. In-hospital mortality rates are very high, ranging from 35% to greater than 50%, dependent on the severity of hypoxemia. [4 5 6 7 8] Over the last decade, there has been an improvement in survival among patients with ALI treated at ARDS Network centers, suggesting that advancements in critical care accounted for this improvement in mortality. [9]

ARDS remains critically relevant to military medicine today. While patients who do not have pre-existing lung disease with ARDS can regain excellent lung function, challenges remain in ensuring survival through the initial associated hypoxemia or hypercarbia and in obtaining return to full function through rehabilitation. Of particular concern are the reports of combat casualties with severe ARDS in young, otherwise healthy, injured military personnel during current operations, some related to incendiary device blast injury.

The current analysis was performed to examine ALI and ARDS in combat casualty care. The primary objectives of this study were threefold: *First*, to assess the epidemiology of ALI/ARDS in military combat casualties; *Second*, to determine risk factors for ALI/ARDS in combat casualty care; *Third*, to examine outcome in ALI/ARDS patients.

Methods

The Joint Theater Trauma Registry (JTTR) was queried for the period October 7, 2001 through August 2, 2008 GWOT to determine necessary data elements for ALI/ARDS and disease-specific outcome variables. Queries were designed to determine specific risk factors for ALI/ARDS in combat casualty, to investigate transfusion, blast injury and altitude as specific risk factors for ALI/ARDS in combat casualty and to review current treatment of ALI/ARDS and short-term and long-term outcomes. Data released was limited as felt to be necessary for sensitive military information. The initial query returned with the subset of patients meeting potential ARDS criteria (n=127), reflecting inadequate sample size for appropriate statistical analyses. Description of this cohort is summarized in the following tables. Data in many cases was incomplete. A second request for repeat query for further information was made. Data analysis was substantially enhanced by the revised query.

- Military IRB Approval for JTTR data queries obtained
- Civilian-Military Inter-service collaborations established
- JTTR data dictionary reviewed for ALI/ARDS data elements and disease-specific outcome variables
- JTTR query designed to identify subset of patients with ALI/ARDS
- Query performed and limited data set released to civilian investigators
- Outcomes of critical care and ventilator support identified
- Second query generated, with additional information requested from the Transfusion database
- Participated in ATAAC presentation and review of ARDS paper

As this grant represented a new collaborative effort between military and civilian investigators, infrastructure and processes were built to facilitate appropriate interaction. IRB approval was obtained through the Military IRB and interservice collaborators identified. The initial proposals were accepted and JTTR data dictionary definitions were released to civilian investigators for review. We found that specific variables relevant to the AECC ARDS definition are not routinely captured in the JTTR (P/F ratio to assess severity of ARDS, radiology report of chest radiographs). CPT and ICD-9 codes and complications are routinely captured and a query was designed to capture elements of respiratory failure, requirements for ventilator support and critical care, specific codes for ARDS.

Results

The query yielded 4666 individuals with 4700 separate records. 152 ARDS cases (3.2% of total cohort) were identified; overall mortality was 12.6%. No difference in age was identified between ARDS, Non-ARDS intubated and non-intubated patients. Univariate analysis confirmed that female gender (5.2 vs. 2.2%, $p<0.05$), increasing ISS (ISS $\geq$ 25 in 36.8% of ARDS patients vs. 27.0% in non-ARDS intubated group and 2.6% in non-intubated control cohort, $p<0.05$), decreasing systolic blood pressure (SBP) and decreased Glasgow coma scale (GCS) score were risk factors for ARDS. Multiple logistic regression analysis confirmed that ARDS was associated with female gender (OR 2.384, 95% CI 1.052-5.401, p=0.037), higher ISS (OR 0.226, 95% CI 0.140-0.365, $p<0.0001$ for ISS $<$ 15 vs. $\geq$ 25), and shock (SBP $<$ 90 vs $\geq$ 90, OR 1.937, CI 1.183-3.169, p=0.0086) at the first point of medical care.

Critical care resource utilization was significant higher in patients with ARDS. Ventilator days (7.1 vs. 3.7 mean days), ICU days (11.2 vs. 5.6 mean days) and hospital length of stay (LOS) (11.0 vs. 5.0 mean days) were significantly increased in the ARDS patient group. Mortality was significantly higher in the ARDS cohort (12.6%) compared to non-ARDS intubated patients (8.8%) and the non-intubated cohort (3.2%).

Multiple logistic regression analysis also confirmed that ARDS was an independent risk factor for death (OR 4.847, 95% CI 2.411-9.743, $p<0.0001$ for ARDS vs. Non-ARDS intubated). Additional independent risk factors for death in this cohort were increased injury severity measured by ISS, decreased SBP reflective of shock state, and decreased admission GCS.

Univariate Analysis – Risk Factors for ARDS:

Risk Factor		OR Point Estimate	OR 95% Wald Confidence Limits		P-value
GENDER	Female vs Male	2.240	1.073	4.680	0.032
AGE	26-35 vs >46	2.276	0.309	16.761	0.88
	36-45 vs >46	2.151	0.278	16.617	
	<=25 vs >46	2.270	0.312	16.522	
INJURY CAUSE	Blast vs Penetrating	1.414	0.895	2.232	0.49
	Blunt vs Penetrating	1.204	0.637	2.273	
	Other vs Penetrating	1.139	0.427	3.036	
Mil ISS	14-24 vs >=25	0.743	0.494	1.118	<.0001
	<15 vs >=25	0.160	0.105	0.242	
Mil ISS (Continuous)	One unit increase of ISS	1.024	1.018	1.030	<.0001
SBP	<90 vs >=90	3.096	1.933	4.960	<.0001
GCS TOTAL	13-15 vs 9-12	0.421	0.219	0.810	<.0001
	3-8 vs 9-12	1.002	0.517	1.945	
GCS TOTAL (Continuous)	One unit increase of GCS	0.933	0.905	0.961	<.0001

Multiple Logistic Regression Analysis – Risk Factors for ARDS:

Risk Factor		OR Point Estimate	OR 95% Wald Confidence Limits		P-value
Age (continous)	One year increase in age	1.006	0.980	1.032	0.67
GENDER	Female vs Male	2.384	1.052	5.401	0.037
INJURY CAUSE	Blast vs Penetrating	1.220	0.751	1.980	0.36
	Blunt vs Penetrating	1.634	0.829	3.218	
	Other vs Penetrating	2.185	0.711	6.714	
Mil ISS	14-24 vs >=25	0.839	0.540	1.303	<.0001
	<15 vs >=25	0.226	0.140	0.365	
SBP	<90 vs >=90	1.937	1.183	3.169	0.0086
GCSTOTAL	13-15 vs 9-12	0.654	0.334	1.281	0.14
	3-8 vs 9-12	0.938	0.477	1.843	

Univariate Analysis – Risk Factors for Death:

Risk Factor		OR Point Estimate	OR 95% Wald Confidence Limits		P-value
GENDER	Female vs Male	0.818	0.357	1.876	0.64
AGE	26-35 vs >46	1.258	0.386	4.093	0.32
	36-45 vs >46	1.831	0.547	6.123	
	<=25 vs >46	1.415	0.440	4.546	
INJURY CAUSE	Blast vs Penetrating	0.915	0.684	1.224	0.0059
	Blunt vs Penetrating	0.458	0.271	0.771	
	Other vs Penetrating	0.384	0.152	0.967	
Mil ISS	14-24 vs >=25	0.406	0.291	0.568	<.0001
	<15 vs >=25	0.084	0.060	0.119	
Mil ISS (Continuous)	One unit increase of ISS	1.040	1.035	1.044	<.0001
SBP	<90 vs >=90	12.243	8.836	16.963	<.0001
GCS TOTAL	13-15 vs 9-12	0.159	0.078	0.326	<.0001
	3-8 vs 9-12	3.782	2.016	7.094	
GCS TOTAL (Continuous)	One unit increase of GCS	0.764	0.740	0.790	<.0001
ARDS	ARDS vs Neither	4.295	2.521	7.317	<.0001
	NON-ARDS Intubated vs Neither	2.874	2.187	3.778	
	ARDS vs NON-ARDS Intubated	1.494	0.904	2.471	

Multiple Logistic Regression Analysis – Risk Factors for Death:

Risk Factor		OR Point Estimate	OR 95% Wald Confidence Limits		P-value
Age (continous)	One year increase in age	1.002	0.975	1.030	0.90
GENDER	Female vs Male	1.795	0.580	5.557	0.31
INJURY CAUSE	Blast vs Penetrating	1.024	0.655	1.602	0.52
	Blunt vs Penetrating	0.622	0.280	1.381	
	Other vs Penetrating	1.507	0.394	5.762	
Mil ISS	14-24 vs >=25	0.445	0.267	0.741	<.0001
	<15 vs >=25	0.115	0.060	0.221	
SBP	<90 vs >=90	4.545	2.972	6.952	<.0001
GCSTOTAL	13-15 vs 9-12	0.154	0.063	0.375	<.0001
	3-8 vs 9-12	2.958	1.423	6.150	
ARDS	ARDS vs Neither	0.438	0.183	1.045	<.0001
	NON-ARDS Intubated vs Neither	0.206	0.103	0.415	
	ARDS vs NON-ARDS Intubated	4.847	2.411	9.743	

Univariate Analysis – Risk Factors for ARDS:

Risk Factor		OR Point Estimate	OR 95% Wald Confidence Limits		P-value for OR	Global P-value
GENDER	Female vs Male	2.240	1.073	4.680	0.032	0.032
AGE	26-35 vs >46	2.276	0.309	16.761	0.42	0.88
	36-45 vs >46	2.151	0.278	16.617	0.46	
	<=25 vs >46	2.270	0.312	16.522	0.42	
INJURY CAUSE	Blunt vs BLAST	0.851	0.506	1.432	0.54	0.49
	Other vs BLAST	0.805	0.324	2.001	0.64	
	Penetrating vs BLAST	0.707	0.448	1.117	0.14	
Mil ISS	14-24 vs >=25	0.743	0.494	1.118	0.15	<.0001
	<15 vs >=25	0.160	0.105	0.242	<.0001	
Mil ISS (Continuous)	One unit increase of ISS	1.024	1.018	1.030	<.0001	<.0001
SBP	<90 vs >=90	3.096	1.933	4.960	<.0001	<.0001
GCS TOTAL	13-15 vs 9-12	0.421	0.219	0.810	0.0095	<.0001
	3-8 vs 9-12	1.002	0.517	1.945	1.00	
GCS TOTAL (Continuous)	One unit increase of GCS	0.933	0.905	0.961	<.0001	<.0001

Multiple Logistic Regression Analysis – Risk Factors for ARDS:

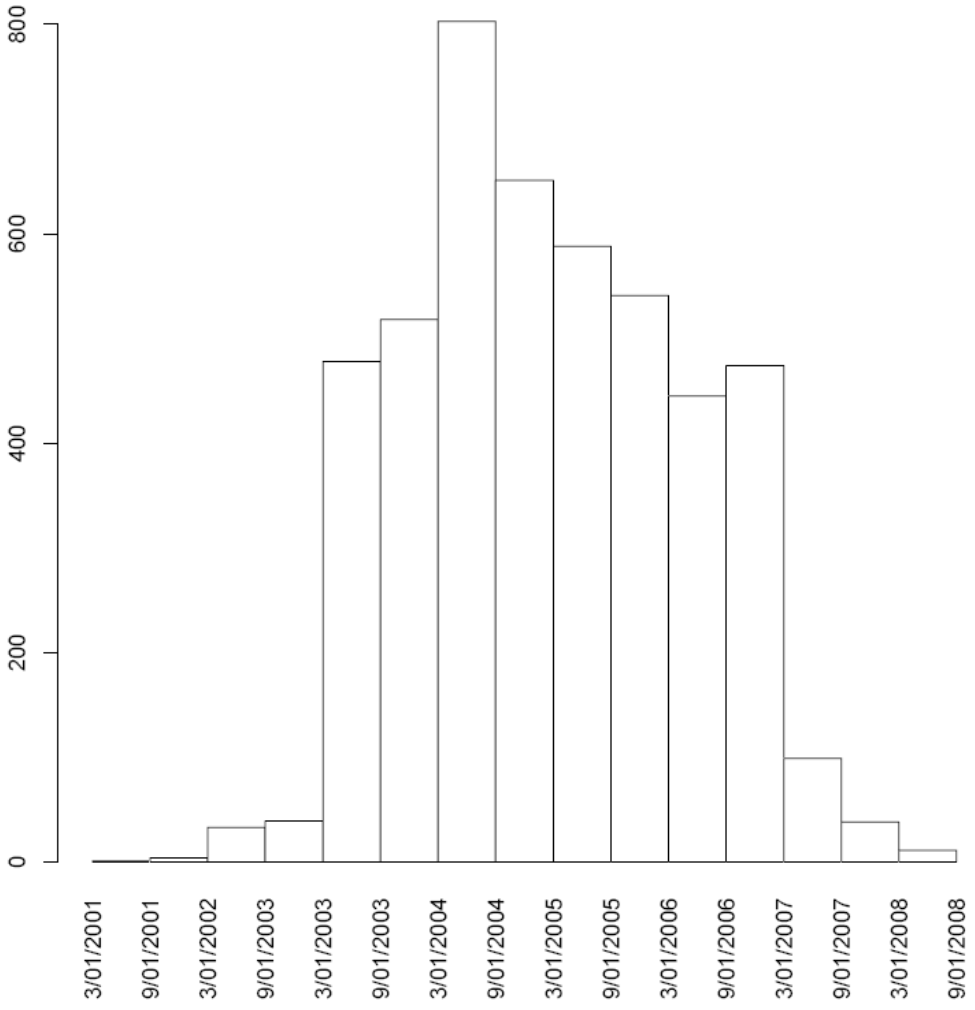
Risk Factor		OR Point Estimate	OR 95% Wald Confidence Limits		P-value for OR	P-value
Age (continous)	One year increase in age	1.006	0.980	1.032	0.67	0.67
GENDER	Female vs Male	2.384	1.052	5.401	0.037	0.037
INJURY CAUSE	Blunt vs BLAST	1.339	0.770	2.331	0.30	0.36
	Other vs BLAST	1.792	0.625	5.138	0.28	
	Penetrating vs BLAST	0.820	0.505	1.331	0.42	
Mil ISS	14-24 vs >=25	0.839	0.540	1.303	0.43	<.0001
	<15 vs >=25	0.226	0.140	0.365	<.0001	
SBP	<90 vs >=90	1.937	1.183	3.169	0.0086	0.0086
GCSTOTAL	13-15 vs 9-12	0.654	0.334	1.281	0.22	0.14
	3-8 vs 9-12	0.938	0.477	1.843	0.85	

Results of First Data Query from JTTR

Date of Injury

A total of 127 unique individuals with 137 separate records were identified. The majority of cases identified occurred before 06/05, with an apparent decrease in reporting to less than 15 incident cases per 6 month period between 1/05 and 3/08.

Figure1. Date of injury



Mechanism of Injury

The primary mechanism of injury was blast and blunt injury, similar to that reported for the all casualties in OIF, accounting for 80% of patients.

Mechanism of Injury (n=127)

Mechanism of Injury	Frequency	Percent
Blast	82	64.57
Blunt	20	15.75
Disease	2	1.57
Drowning	2	1.57
Machinery	1	0.79
Penetrating	20	15.75

Method of Transportation

No patient had multiple records at the same level of care. Med Evac Air was the main method of transportation of these patients. Only two subjects had used Med Evac Ground as method of transportation.

Method of transportation for subjects with record from one level of care (n=117)

Level of care	Method of transport	N
III	Med Evac Air	11
	Not Documented	4
IIb	Med Evac Ground	1
	Not Documented	1
IV	Carried	2
	Med Evac Air	64
	Not Documented	9
Vs	Not Documented	25

Method of transportation for subjects with record from multiple levels of care (n=10)

Case ID	Enroute	IV	Vs	II
8598		Med Evac Air		
13402		Med Evac Air	Not Documented	
21862	Med Evac Air	Med Evac Air		
22674	Med Evac Air	Med Evac Air		
27166		Med Evac Air		Med Evac Air
28229	Med Evac Air		Not Documented	
30589	Med Evac Air		Not Documented	
30609		Med Evac Air	Not Documented	
35551	Med Evac Air			Med Evac Air
40362		Med Evac Air Med Evac Ground		Med Evac Air

First Level of Care

The majority of the patients were first identified after initial stabilization, with 86.67% of cases first identified at level IV or Vs facilities and the majority at a single level IV facility.

First level of care (n=127)

Level of Care	Frequency	Percent
Enroute	5	2.36
III	18	13.39
IIb	2	1.57
IV	78	62.20
Vs	25	20.47

First level of care and MTF (n=127)

Level of Care	MTF name	Frequency	Percent
Enroute	CCATT	5	100.00
IIb	FST	2	100.00
III	28th CSH Baghdad	1	5.56
	31st CSH Baghdad	5	27.78
	325th FH Bagram	1	5.56
	332nd EMDG	6	33.33
	47th CSH	1	5.56
	67th CSH Tikrit	1	5.56
	86th CSH Baghdad	3	16.67
IV	LRMC	77	100.00
Vs	BAMC	2	8
	WRAMC	23	92

Multiple Levels of Care

Among the 127 subjects, records were available from multiple levels of care for only 10 subjects. It appears that this is an artifact of the data retrieval and that only specific phases of care where respiratory failure developed where included in the cohort.

Level of care, MTF and disposition date for the 10 subjects with records at multiple levels of care.

Case ID	Date wounded	Level of care	MTF name	Disposition date	Number of levels of care
8598	5-May-03	Enroute	CCATT	6-May-03	2
8598	5-May-03	IV	LRMC	7-May-03	
13402	30-Aug-03	IV	LRMC	4-Sep-03	2
13402	30-Aug-03	Vs	WRAMC	7-Sep-03	
21862	7-Oct-04	IV	LRMC	11-Oct-04	2
21862	7-Oct-04	Enroute	CCATT	9-Oct-04	
22674	27-Oct-04	Enroute	CCATT	28-Oct-04	2
22674	27-Oct-04	IV	LRMC	28-Oct-04	
27166	2-Jan-05	III	86th CSH Baghdad	3-Jan-05	2
27166	2-Jan-05	IV	LRMC	5-Jan-05	
28229	3-May-05	Enroute	CCATT	4-May-05	2
28229	3-May-05	Vs	BAMC	7-Jul-05	
30589	19-Jun-05	Vs	WRAMC	14-Jul-05	2
30589	19-Jun-05	Enroute	CCATT	21-Jun-05	
30609	14-Jun-05	IV	LRMC	28-Jun-05	2
30609	14-Jun-05	Vs	WRAMC	29-Aug-05	
35551	14-Mar-05	III	332nd EMDG	17-Mar-05	2
35551	14-Mar-05	Enroute	CCATT	18-Mar-05	
40362	23-May-05	IV	LRMC	15-Jun-05	3
40362	23-May-05	IV	LRMC	21-Jun-05	
40362	23-May-05	III	332nd EMDG	31-May-05	

Note:

Subject 40362 has two records from the same hospital with different disposition dates. Some of the variables differ between these two records, including method of transportation.
For subject 22674, the disposition date from Enroute and IV hospitals are the same.

Arrival and Discharge Status

One ER death was recorded at the 86th CSH, in a patient who sustained blunt injury, ISS 10. The remaining patients formed the basis for the remainder of the analysis.

Arrival Status (n=127)

Arrival Status	Frequency	Percent
Alive	126	99.21
Died	1	0.79

Nine patients died as inpatients (7.1%), 93 survived for transfer to another facility, 19 returned to duty after transfer to the Level V facility and 1 was on medical hold. Disposition was not documented for four patients in the JTTR.

Discharge Disposition by Level of Care for Subjects with Only 1 Record (n=117)

Level of Care	Discharge Disposition								
Frequency	CRO-ER DEATH	DIED-INPATIENT STAY	DISCH-OTHER FED FACIL	Not Documented	RETURNED TO DUTY	TRANSFERED-AIR FORCE	TRANSFERED-ARMY MTF	TRANSFERED-NAVY MTF	Total
III	1	0	0	0	0	4	9	1	15
IIb	0	0	0	0	0	0	2	0	2
IV	0	4	0	4	0	10	47	10	75
Vs	0	3	3	0	18	0	1	0	25
Total	1	7	3	4	18	14	59	11	117

Discharge disposition for subjects with records at multiple levels of care

CaseID	Enroute	IV	Vs	III
8598	TRANSFERED-ARMY MTF	TRANSFERED-ARMY MTF		
13402		TRANSFERED-ARMY MTF	DIED-INPATIENT STAY	
21862	TRANSFERED-ARMY MTF	TRANSFERED-ARMY MTF		
22674	TRANSFERED-ARMY MTF	TRANSFERED-ARMY MTF		
27166		TRANSFERED-ARMY MTF		TRANSFERED-AIR FORCE
28229	TRANSFERED-ARMY MTF		MEDICAL HOLD	
30589	TRANSFERED-ARMY MTF		DIED-INPATIENT STAY	
30609		TRANSFERED-ARMY MTF	RETURNED TO DUTY	
35551	TRANSFERED-ARMY MTF			TRANSFERED-ARMY MTF
40362		TRANSFERED-ARMY MTF		TRANSFERED-ARMY MTF

Duration from Injury to Disposition

Time recorded from initial injury to disposition to definitive care in this cohort was excellent, with stays ranging on, average, less than 2 days at combat support hospitals, 8 days at the level II trauma center (LRMC) and 44 days at stateside hospitals. Data is captured in increments of dates, some stays are likely much less than 24 hours at the combat support hospitals.

Duration from injury to disposition by level of care (n=138)

Level of care	N Obs	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum
Enroute	6	1.8	1.2	1.5	1.0	2.0	1.0	4.0
III	18	1.7	1.9	1.0	1.0	2.0	0.0	8.0
IIb	2	0.0	0.0	0.0	0.0	0.0	0.0	0.0
IV	83	7.7	8.0	5.0	3.0	8.0	1.0	38.0
Vs	29	44.2	24.4	41.0	30.0	55.0	5.0	107.0

The overall time from injury to last disposition was 15 days.

Duration from injury to last disposition in the record (n=127)

N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum
127	15.0	20.8	5.0	3.0	19.0	0.0	107.0

Ventilator support and Critical Care support days

Days on ventilator support for the cohort document that the mean time on ventilator at level II b and III hospitals was similar to total time at the facility, suggesting the need for continued ventilatory support through transfer to higher levels of care. The requirement for ventilator support largely drove the total days of critical care support at all levels.

It is important to note that 10 patients, ***despite having diagnoses listed as respiratory failure***, are listed as having 0 days of ventilator support. It is unclear if this is related to respiratory failure occurring at another point during the continuum of care and no ventilation was administered on the available record or if this reflects data entry omissions. One patient died in the Emergency Room and potentially might not have had a full day of ventilator support recorded. Another patient is listed as having >96 hours mechanical ventilator support but 0 ventilator days are recorded.

Number of ventilator support days by level of care (n=138)

Level of Care	N Obs	N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum	N Miss
Enroute	6	5	1.0	0.0	1.0	1.0	1.0	1.0	1.0	1
III	18	18	2.2	1.9	2.0	2.0	2.0	0.0	8.0	0
IIb	2	2	0.5	0.7	0.5	0.0	1.0	0.0	1.0	0
IV	83	81	5.0	4.7	3.0	3.0	6.0	0.0	27.0	2
Vs**	29	1	0.0	.	0.0	0.0	0.0	0.0	0.0	28

***NOTE: Ventilator support days at the Vs hospitals was not routinely required by the JTTR.*

Number of critical care support days by level of care (n=138)

Level of Care	N Obs	N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum	N Miss
Enroute	6	5	1.0	0.0	1.0	1.0	1.0	1.0	1.0	1
III	18	18	2.2	1.9	2.0	2.0	2.0	0.0	8.0	0
IIb	2	2	0.5	0.7	0.5	0.0	1.0	0.0	1.0	0
IV	83	82	5.8	5.8	4.0	3.0	6.0	0.0	34.0	1
Vs	29	29	13.3	12.6	11.0	5.0	14.0	0.0	48.0	0

List of subjects whose number of vent support day = 0

Case ID	Level of care	MTF name	Number of vent support days	Arrival status	Discharge disposition
9351	III	47th CSH	0	Alive	TRANSFERED-NAVY MTF
55963	III	86th CSH Baghdad	0	Alive	CRO-ER DEATH
19333	IIb	FST	0	Alive	TRANSFERED-ARMY MTF
13851	IV	LRMC	0	Alive	TRANSFERED-ARMY MTF
15691	IV	LRMC	0	Alive	TRANSFERED-ARMY MTF
19556	IV	LRMC	0	Alive	TRANSFERED-ARMY MTF
31082	IV	LRMC	0	Alive	TRANSFERED-ARMY MTF
34357	IV	LRMC	0	Alive	TRANSFERED-ARMY MTF
40362	IV	LRMC	0	Alive	TRANSFERED-ARMY MTF
17781	Vs	BAMC	0	Alive	DIED-INPATIENT STAY

Number of vent support days for subjects with record from only one level of care (n=117)

N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum	N Miss
93	4.3	4.5	3.0	2.0	5.0	0.0	27.0	24

*Please note that this summary is over different levels of care for **ventilator support** days.*

Number of critical care support days for subjects with record from only one level of care (n=117)

N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum	N Miss
117	6.6	7.8	4.0	2.0	8.0	0.0	48.0	0

*Please note that this summary is over different level of care for number of **critical care support** days.*

Total number of vent support days for all subjects

If a subject has records from multiple levels of care, they are summed up to calculate "total number of vent support days". From the table on the previous page, one can see that for 6 of the 10 subjects with records from multiple levels of care, we are not able to calculate the total because of missing values.

N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum	N Miss
97	4.5	4.7	3.0	2.0	5.0	0.0	27.0	25

Total number of critical care support days for all subjects

If a subject has records from multiple levels of care, they are summed up to calculate "total number of critical care support days". From the first table on the previous page, one can see that for 2 of the 10 subjects with records from multiple levels of care, we are not able to calculate the total because of missing values.

N	Mean	Std Dev	Median	Lower Quartile	Upper Quartile	Minimum	Maximum	N Miss
125	7.1	8.7	4.0	2.0	8.0	0.0	48.0	0

Number of vent support days by level of care for subjects with multiple records

Case ID	Level of care	MTF name	Number of vent support days
8598	Enroute	CCATT	1
8598	IV	LRMC	Not Documented
13402	IV	LRMC	4
13402	Vs	WRAMC	Not Documented
21862	IV	LRMC	3
21862	Enroute	CCATT	1
22674	Enroute	CCATT	1
22674	IV	LRMC	Not Documented
27166	III	86th CSH Baghdad	2
27166	IV	LRMC	2
28229	Enroute	CCATT	1
28229	Vs	BAMC	Not Documented
30589	Vs	WRAMC	Not Documented
30589	Enroute	CCATT	Not Documented
30609	IV	LRMC	12
30609	Vs	WRAMC	Not Documented
35551	III	332nd EMDG	2
35551	Enroute	CCATT	1
40362	IV	LRMC	13
40362	IV	LRMC	0
40362	III	332nd EMDG	8

Number of critical care support days by level of care for subjects with multiple records

Case ID	Level of Care	MTF_name	Number Critical Care Support Days
8598	Enroute	CCATT	1
8598	IV	LRMC	Not Documented
13402	IV	LRMC	4
13402	Vs	WRAMC	1
21862	IV	LRMC	3
21862	Enroute	CCATT	1
22674	Enroute	CCATT	1
22674	IV	LRMC	4
27166	III	86th CSH Baghdad	2
27166	IV	LRMC	2
28229	Enroute	CCATT	1
28229	Vs	BAMC	46
30589	Vs	WRAMC	20
30589	Enroute	CCATT	Not Documented
30609	IV	LRMC	12
30609	Vs	WRAMC	5
35551	III	332nd EMDG	2
35551	Enroute	CCATT	1
40362	IV	LRMC	15
40362	IV	LRMC	7
40362	III	332nd EMDG	8

ICD9 codes

ICD9 codes formed the basis of the initial data query from the JTTR to identify respiratory failure and possible ALI or ARDS. At least one pulmonary insufficiency code was present in all patients in this initial JTTR query.

There are 3 common methods used to detect ARDS: Clinical screening, chart review and diagnostic coding. Since we will be using the JTTR, clinical screening and chart review are not feasible. We can use the American European Consensus Conference definition of ARDS (PaO2/FiO2 ratio less than 200 and noncardiogenic bilateral pulmonary infiltrates) and ALI (PaO2/FiO2 ratio less than 300), but it was determined that these data (arterial blood gas data and chest radiograph findings) are **NOT** routinely available in the JTTR.

ICD-9 codes can be utilized as well to identify patients with possible ALI or ARDS.

518.5 includes pulmonary insufficiency following trauma and surgery, ARDS, pulmonary insufficiency following shock, surgery, trauma, shock lung. This code excludes ARDS associated with other conditions (518.82) and pneumonia.

518.82 includes other pulmonary insufficiency, not elsewhere classified, acute respiratory distress, acute respiratory insufficiency, ARDS not elsewhere classified. This code excludes ARDS associated with trauma or surgery (518.85), pumonary insufficiency following trauma or surgery (518.85).

518.81 includes respiratory failure, acute and/or chronic. Excludes: Acute respiratory distress (518.82), respiratory arrest (799.1).

It was not clear whether these ICD-9 codes were available in the JTTR. Alternatively, the ICD-9 codes of 518.81, 518.5 and 518.82 can be cross-referenced with the procedural codes for ventilatory support (96.70, 96.71, 96.72). This search may increase the yield of patients with possible ALI and ARDS since coders may not include the codes for ARDS if they do not see if written in the patient progress notes clearly. Furthermore, we know that clinicians underdiagnose ALI and ARDS. An initial query to just pull the number of patients with these codes might be useful. But all other queries must include all the other trauma data elements present in the JTTR as potential risk factors or treatment factors that may impact on the incidence of ALI/ARDS and all-cause outcome.

Alternatively, the initial search can be for all intubated and mechanically ventilated patients in the JTTR, or for all patients with ICD-9 codes 518.5 and 518.82 without additional constraint. The ICD-9 code 518.81 may not be searched because its descriptors do not include ARDS, but there may be errors in coding that should be considered. The second search can incorporate the same ICD-9 codes (518.5 and 518.82) with the additional mandate of ventilatory support (procedural codes 96.70, 96.71 and 96.72, established in 1991). Some studies have suggested that this combination of ICD-9 disease and procedure codes representing the ICD-9 ARDS criteria mandates that the ARDS patient must meet all of the following criteria:

1. Have a code directly indicated ARDS in the ICD-9 description;
2. Be on concurrent ventilatory support, and
3. Have required >/= 4 days of ventilatory support unless the disease was fatal within that time (lower limit) or have required ventilatory support of unspecified duration, survivors and nonsurvivors (upper limit).

A total of 117 patients had ICD-9 codes for acute respiratory failure or pulmonary insufficiency which can be used to identify a patient cohort with possible ALI or ARDS.

List of subjects with record from only one level of care (n=117)

Codes	Code description	N	Total
518.5	POST TRAUM PULM INSUFFIC	7	48
	POST TRAUM PULM INSUFFICIEN	41	
518.81	ACUTE RESPIRATRY FAILURE	9	46
	RESPIRATORY FAILURE	37	
518.82	OTH PULMONARY INSUFFICIENCY	14	23
	OTHER PULMONARY INSUFF	8	
	OTHER PULMONARY INSUFFICIENCY	1	

List of subjects with records from multiple levels of care

Case ID	Level of care	Codes	Code description
8598	Enroute	.	
8598	IV	518.81	RESPIRATORY FAILURE
13402	IV	518.5	POST TRAUM PULM INSUFFIC
13402	Vs	518.81	RESPIRATORY FAILURE
21862	Enroute	.	
21862	IV	518.5	POST TRAUM PULM INSUFFICIEN
22674	Enroute	.	
22674	IV	518.82	OTH PULMONARY INSUFFICIENCY
27166	III	518.81	RESPIRATORY FAILURE
27166	III	518.82	OTHER PULMONARY INSUFFICIENCY
27166	IV	518.81	RESPIRATORY FAILURE
28229	Enroute	.	
28229	Vs	518.5	POST TRAUM PULM INSUFFICIEN
30589	Enroute	.	
30589	Vs	518.5	POST TRAUM PULM INSUFFICIEN
30609	IV	518.5	POST TRAUM PULM INSUFFICIEN
30609	Vs	518.5	POST TRAUM PULM INSUFFICIEN
35551	Enroute	.	
35551	III	518.5	POST TRAUM PULM INSUFFICIEN
40362	III	518.5	POST TRAUM PULM INSUFFICIEN
40362	IV	518.5	POST TRAUM PULM INSUFFICIEN

CPT Codes

CPT codes identified ICU-related and respiratory failure-related procedures which may be associated with ARDS. Of patients where a mechanical ventilation code was specified (n=63), almost 50% specified treatment for greater than 96 hours. Tracheostomy was performed in 18% of the entire patient cohort.

CPT codes for subjects with record only at one level of care (10 subjects had multiple CPT codes).

Number	Code	N
31.1	TEMPORARY TRACHEOSTOMY	18
33.21	BRONCHOSCOPY THRU STOMA	4
33.22	FIBER-OPTIC BRONCHOSCOPY	2
33.23	OTHER BRONCHOSCOPY	17
34.04	INSERT INTERCOSTAL CATH	14
519.01	TRACHEOSTOMY INFECTION	1
519.02	TRACHEOSTOMY MECH COMPLICTN	1
584.5	LOWER NEPHRON NEPHROSIS	2
584.9	ACUTE RENAL FAILURE NOS	1
	ACUTE RENAL FAILURE UNSPEC	1
785.52	SEPTIC SHOCK	1
958.4	TRAUMATIC SHOCK	4
96.7	CONT MECH VENT-UNSPC DUR	2
	CONT MECH VENT-UNSPEC DUR	2
96.71	CONT MECH VENT < 96 HRS	25
	CONT MECH VENTRICULAR < 96 HRS	5
96.72	CONT MECH VENT 96+ HRS	28
	CONT MECH VENTRICULAR 96+ HRS	1
99.63	CLOSED CHEST CARD MASSAGE	1
997.3	SURG COMP-RESPIR SYST	1
	SURG COMPLIC RESPIR SYST	4
NULL	NULL	1

Thirty-two subjects have multiple CPT codes at the same level of care.

Among them, five have records at multiple levels of care (See the table below).

List of subjects with records from multiple levels of care

Case ID	Level of care	CTP code	Description
8598	Enroute	31.1	TEMPORARY TRACHEOSTOMY
8598	IV	31.1	TEMPORARY TRACHEOSTOMY
13402	IV	96.72	CONT MECH VENT 96+ HRS
13402	Vs	96.71	CONT MECH VENT < 96 HRS
21862	Enroute	96.7	CONT MECH VENT NFS
21862	IV	96.71	CONT MECH VENT < 96 HRS
22674	Enroute	96.7	CONT MECH VENT NFS
22674	IV	33.23	OTHER BRONCHOSCOPY
27166	III	96.71	CONT MECH VENTRICULAR < 96 HRS
27166	IV	96.71	CONT MECH VENT < 96 HRS
28229	Enroute	96.71	CONT MECH VENT < 96 HRS
28229	Vs	31.1	TEMPORARY TRACHEOSTOMY
28229	Vs	96.72	CONT MECH VENT 96+ HRS
30589	Enroute		
30589	Vs	31.1	TEMPORARY TRACHEOSTOMY
30589	Vs	584.9	ACUTE RENAL FAILURE UNSPEC
30609	IV	33.23	OTHER BRONCHOSCOPY
30609	IV	96.72	CONT MECH VENT 96+ HRS
30609	Vs	31.1	TEMPORARY TRACHEOSTOMY
30609	Vs	96.72	CONT MECH VENT 96+ HRS
35551	Enroute	96.7	CONT MECH VENT NFS
35551	Enroute	994.1	Drowning
35551	III		
40362	III	33.23	OTHER BRONCHOSCOPY
40362	III	34.04	INSERT INTERCOSTAL CATH
40362	IV		
40362	IV	96.72	CONT MECH VENTRICULAR 96+ HRS

Complications

Complications were identified in 26 of 127 patients (20.5% of the total patient cohort). Some patients had multiple complications listed across multiple levels of care. Note that "ARDS" is specifically listed in only 6 patients in the cohort which may reflect underdiagnosis or omissions of documentation, recognizing limitations of data collection and coding at scene. Data is missing on 105 patients.

Complications for subjects with record at only one level of care
(20 subjects had complications)

complications	N
ARDS	6
ASPIRATION PNEUMONIA	2
Acute Renal Failure	1
Acute Respiratory Failure	2
Anemia/Blood Loss	2
Atelectasis	2
C. Diff Colitis	1
Coagulopathy	2
None	1
Not Documented	105
PNEUMONIA	12
PNEUMOTHORAX	7
Pleural Effusion	2
Pneumonia	2
Soft Tissue Infection	1

Ten (10) patients had multiple complications at multiple levels of care

Twenty-one *subjects had multiple complications record at the same level of care. Among them three subjects (13402, 22674, and 40362) have records from multiple levels of care (See the table below). The rest of the subjects only have records from one level of care.*

Complications for subjects with records at multiple levels of care

casid	Level of care	complications
8598	Enroute	Not Documented
8598	IV	Not Documented
13402	IV	Not Documented
13402	IV	PNEUMONIA
13402	Vs	Not Documented
21862	Enroute	None
21862	IV	Not Documented
22674	Enroute	anemia/blood loss
22674	Enroute	Coagulopathy
22674	Enroute	esophageal intubation
22674	IV	ASPIRATION PNEUMONIA
22674	IV	Not Documented
27166	III	Not Documented
27166	IV	PNEUMONIA
28229	Enroute	Not Documented
28229	Vs	Not Documented
30589	Enroute	Hypotension
30589	Vs	Not Documented
30609	IV	PNEUMONIA
30609	Vs	Not Documented
35551	Enroute	Not Documented
35551	III	Not Documented
40362	III	Not Documented
40362	IV	Not Documented
40362	IV	PNEUMONIA

Vasopressors: The majority of patients in the cohort did not require vasopressors (113/117).

Vasopressors for subjects with records from only one level of care

Vasopressors	N
DOBUTAMINE	1
DOPAMINE	1
EPINEPHRINE	4
LEVATERENOL BITARTRATE	1
NONE	113
Not Documented	4
PHENYLEPHRINE	6
VASOPRESSIN (ADH)	2

Vasopressors for subjects with records from multiple levels of care (n=8)

casid	Level of care	vasopressors
8598	Enroute	Not Documented
8598	IV	NONE
13402	IV	NONE
13402	Vs	NONE
21862	Enroute	Not Documented
21862	IV	NONE
22674	Enroute	Not Documented
22674	IV	NONE
27166	III	NONE
27166	IV	NONE
28229	Enroute	Not Documented
28229	Vs	NONE
30589	Enroute	Not Documented
30589	Vs	NONE
30609	IV	NONE
30609	Vs	NONE
35551	Enroute	Not Documented
35551	III	NONE
40362	III	DOBUTAMINE
40362	III	NONE
40362	III	PHENYLEPHRINE
40362	IV	NONE

Fluid Amount

Analysis of the relationship of fluid balance to respiratory insufficiency was hampered by multiple inconsistent means of recording fluid input and apparent incomplete data. We now understand that there is a comprehensive transfusion database maintained with the JTTR; if that was not included in the query, it would explain the lack of information in the queried fields. This may require a separate query of the JTTR Transfusion Database for patients at risk for ARDS. Blood transfusion has been identified as an independent risk factor for respiratory failure and ALI/ARDS in civilian trauma studies, and this clearly should be examined in further detail with the JTTR Transfusion Database. This is most important given the recent implementation of aggressive blood transfusion in patients with hemorrhagic shock with 1:1:1 packed red blood cells to fresh frozen plasma to platelet ratios in the combat casualty setting. Significantly higher numbers of patients are now exposed to plasma products, with their associated risk of transfusion-associated acute lung injury (TRALI) and this issue warrants further study.

Fluid amounts for subjects with records at multiple levels of care

Case ID	Level of care	MTF name	Fluid amounts
8598	Enroute	CCATT	Not Documented
8598	IV	LRMC	Not Documented
13402	IV	LRMC	Not Documented
13402	Vs	WRAMC	Not Documented
21862	Enroute	CCATT	Not Documented
21862	IV	LRMC	Not Documented
22674	Enroute	CCATT	Not Documented
22674	IV	LRMC	Not Documented
27166	III	86th CSH Baghdad	Not Documented
27166	IV	LRMC	Not Documented
28229	Enroute	CCATT	2000
28229	Vs	BAMC	Not Documented
30589	Enroute	CCATT	Not Documented
30589	Vs	WRAMC	Not Documented
30609	IV	LRMC	Not Documented
30609	Vs	WRAMC	Not Documented
35551	Enroute	CCATT	1500
35551	III	332nd EMDG	500-2000cc
40362	III	332nd EMDG	>2000cc
40362	IV	LRMC	Not Documented
40362	IV	LRMC	Not Documented

Fluid amount for subjects with record from only one level of care (n=117)

Fluid amounts	Frequency	Percent
3200	1	0.85
3300	1	0.85
4800	1	0.85
500-2000cc	3	2.54
9999	1	0.85
>2000cc	15	12.71
Not Applicable	4	3.39
Not Documented	91	77.97

Fluid amount for subjects with record from only one level of care by level of care (n=117)

Level of Care	Fluid amounts	Frequency	Percent
IIb	>2000cc	1	100.00
III	500-2000cc	3	18.75
	>2000cc	12	75.00
	Not Applicable	1	6.25
IV	3200	1	10.00
	3300	1	10.00
	4800	1	10.00
	9999	1	10.00
	>2000cc	3	30.00
	Not Applicable	3	30.00
	Not Documented	65	86.67
Vs	Not Documented	25	100.00

Blood and Blood Products

Analysis of the relationship of transfusion of blood and blood products to respiratory insufficiency and respiratory failure was not possible due to missing data elements and incomplete data. We now understand that there is a comprehensive transfusion database maintained by some investigators at the JTTR. This was not the data source for blood product transfusion that was included in the query, and therefore explains the lack of information in the queried fields. This may require a separate query of the JTTR Transfusion Database for patients at risk for ARDS. Blood transfusion has been identified as an independent risk factor for respiratory failure and ALI/ARDS in civilian trauma studies, and this clearly should be examined in further detail with the separate JTTR Transfusion Database that we did not have access to. This is most important given the recent implementation of aggressive blood transfusion in patients with hemorrhagic shock with 1:1:1 packed red blood cells to fresh frozen plasma to platelet ratios in the combat casualty setting. Significantly higher numbers of patients are now exposed to plasma products, with their associated risk of transfusion-associated acute lung injury (TRALI) and this issue warrants further study.

Bloodpluscat for subjects with records at multiple levels of care

Case ID	Enroute	IV	Vs	III
8598	Not Documented	None		
13402		None	None	
21862	None	None		
22674	Not Documented	None		
27166		None		None
28229	None		None	
30589	Not Documented		None	
30609		None	None	
35551	Not Documented			None
40362		Not Documented/ Not Documented		Blood Products

Bloodpluscat1 for subjects with record from only one level of care by level of care (n=117)

Level of care	Bloodpluscat1	N
Enroute	Not Documented	3
III	Blood Products	12
	None	2
IIb	None	11

IV	Blood Products	2
	Colloids	62
	None	25
Vs	None	25

Blood pluscats for subjects with records from multiple levels of care.

Case ID	Enroute	IV	Vs	III
8598	Not Documented	None		
13402		None	None	
21862	PRBC	None		
22674	Not Documented	None		
27166		None		None
28229	FFP		None	
30589	Not Documented		None	
30609		None	None	
35551	Not Documented			Not Applicable
40362		Not Documented/ Not Documented		FFP

Blood pluscat2 for subjects with record from only one level of care by level of care (n=117)

Level of care	Blood pluscat2	N
III	Cryoprecipitate (includes Factor VII/VIII)	2
	FFP	1
	None	8
	Not Applicable	3
	Not Documented	1
IIb	None	2

IV	Albumin	2
	FFP	8
	None	59
	Not Applicable	1
	Not Documented	2
	PRBCs	2
	Platelets	1
Vs	None	25

Table of bloodpluscat1 by bloodpluscat2 (n=117)

bloodpluscat1	bloodpluscat2								Total
Frequency	Albumin	Cryoprecipitate (includes Factor VII/VIII)	FFP	None	Not Applicable	Not Documented	PRBCs	Platelets	
Blood Products	0	2	9	0	0	0	2	1	14
Colloids	2	0	0	0	0	0	0	0	2
None	0	0	0	94	4	3	0	0	101
Total	2	2	9	94	4	3	2	1	117

Volume administered by blood product based on all records (n=138)

Blood pluscat2	Volume admin	N
Albumin	200	1
	2031	1
Cryoprecipitate (includes Factor VII/VIII)	150	1
	30	1

FFP	11	1
	1400	1
	1743	1
	2	1
	2025	1
	2403	1
	494	1
	546	1
	660	1
	900	1
	Not Documented	1
None	None	107
Not Applicable	0	5
Not Documented	0	3
	Not Documented	4
PRBC	1	1
PRBCs	259	1
	824	1
Platelets	1	1

Fluid amounts for subjects with more than one record

8598	Not Documented	Not Documented		
13402		Not Documented	Not Documented	
21862	Not Documented	Not Documented		
27166		Not Documented		Not Documented
28229	2000		Not Documented	
30589	Not Documented		Not Documented	
30609		Not Documented	Not Documented	
35551	1500			500-2000cc
40362		Not Documented/ Not Documented		>2000cc

CONCLUSIONS:

ARDS is a potentially lethal condition which remains a potential threat to American combat personnel. It is critically important to understand the incidence, prevalence, epidemiology, risk factors and outcomes from ARDS in combat casualty care.

The JTTR is a remarkable database, collected in the midst of conflict by caregivers whose primary goal is rescue of the war fighter. In order to fully take advantage of its remarkable potential, additional resources must be dedicated to facilitate data collection and analysis of this rich database to advance combat casualty care. Consideration should be given to support of clinical research nurses for consistency and reliability of data acquisition and reliable data entry. There will still be a necessity for chart review in a number of research projects, but improved data in the JTTR would make initial data queries more productive. We understand that at present the process for data collection for the JTTR is currently paper based, but we strongly recommend considering transition to electronic data entry in keeping with the remainder of military initiatives.

Civilian trauma care has always depended on experience gleaned from the military and we are privileged to have had access to the JTTR and to participate in disseminating discoveries. The JTTR will enable the military to collect and synthesize theatre-wide anecdotal experience to a comprehensive database on combat injuries.

We found that data elements for full definition of ARDS (i.e. PaO2/FiO2 ratio, Oxygenation Index, Arterial blood gases, diagnostic radiograph findings) are not currently collected in the JTTR data directory. Utilizing surrogate markers including ICD-9 and CPT codes were utilized to capture a cohort of patients that may have had ALI or ARDS. Additional data analyses are underway and have the potentially to significantly expand the data reviewed in this summary document from our initial query.

OUTLOOK:

We have requested a no-cost extension in order to complete the secondary query and analysis (see attached document that reviews the many challenges that were encountered in this research project). We anticipate that successful evaluation of records along the continuum of care, transfusion data and data from non-ARDS patients will enable us to complete the appropriate comparisons to evaluate risk and prognosis in these injured patients.

ISSUES IDENTIFIED:

Inclusion of ARDS specific data elements

Inclusion of PaO2/FiO2 ratio, results of serial arterial blood gases, results of chest radiograph, mode of mechanical ventilation, ventilator settings. These should all be considered for inclusion in the JTTR, particularly as all move toward electronic medical record capture.

Data organization

Inconsistency in data directory, three separate dictionaries and one supplement

Limited data element availability – inability to obtain data query on control cohort for comparison

Civilian access to confidential information

Delineating availability of database (JTTR, Separate blood transfusion database, CCAT information, other military databases at Bethesda and Walter Reed hospitals, other military branch databases)

Clarification of role of military co-investigators

Mandatory requirement for military PI – Jeremy Cannon- facilitated IRB, superb work ethic. Priority of projects must be delineated. Civilian investigators have no ability to control timeline regarding data queries from the JTTR since these are accomplished by the ISR staff. Consideration should be given to providing raw data to civilian investigators with sensitive data fields deleted, and allowing the civilian investigators to perform their own data queries with their statistical and epidemiologic support at large University settings, including our School of Public Health that has special expertise with large datasets of clinical information with multiple missing data elements.

Coordinating with JTTR access to data elements – must be clarified as to the specific process

The leadership of the JTTR must be made clear to civilian investigators, since attempts at discussing how to obtain data from the JTTR is significantly delayed due to lack of clarity of this important aspect.

Template for accessing JTTR and initiating data query.

We recommend that a document be prepared for any civilian researchers so that they fully understand the process and timeline for obtaining data from the JTTR. This can be accomplished based on our experience with this research proposal and the JTTR queries performed. This document should clearly delineate the limitations of data that will be shared with civilian researchers. Early collaboration with military colleagues and researchers should be mandatory and be established early. All specific documents that are required for IRB approval should be provided to the PIs well in advance of initiation of the research proposal. Delineation of this information for all future researchers that request data from the JTTR would be a tremendous advance for the future.

Continuum of care not represented in JTTR

Collaboration with other military researchers that can provide data from other military databases that would augment the JTTR (Bethesda Naval Medical Center, James Dunne MD and others).

Key Research Accomplishments

- 1: Review Joint Theater Trauma Registry (JTTR) and Data Dictionary to determine necessary data elements for ALI/ARDS and disease-specific outcome variables
- 2: Review JTTR to determine specific risk factors for ALI/ARDS in combat casualty
- 3: Review JTTR to investigate blood transfusion as a specific risk factor for ALI/ARDS in combat casualty
- 4: Review JTTR to investigate Bomb Blast Injury as a specific risk factor for ALI/ARDS in combat casualty, particularly with regard to severity of ARDS
- 5: Review of ALI/ARDS epidemiology and outcomes in combat casualty using JTTR and additional data sources as necessary
- 6: Review of all deaths in combat casualty using JTTR and additional data sources as necessary to determine whether ALI/ARDS was a contributing cause

Reportable Outcomes

Abstract accepted for presentation at upcoming American Association for Surgery of Trauma (AAST) Annual Meeting, September 2009.

Manuscript submitted for publication to Journal of Trauma based on presentation at AAST annual meeting September 2009.

Conclusions

The query yielded 4666 individuals with 4700 separate records. 152 ARDS cases (3.2% of total cohort) were identified; overall mortality was 12.6%. No difference in age was identified between ARDS, Non-ARDS intubated and non-intubated patients. Univariate analysis confirmed that female gender (5.2 vs. 2.2%, $p<0.05$), increasing ISS (ISS $\geq$ 25 in 36.8% of ARDS patients vs. 27.0% in non-ARDS intubated group and 2.6% in non-intubated control cohort, $p<0.05$), decreasing systolic blood pressure (SBP) and decreased Glasgow coma scale (GCS) score were risk factors for ARDS. Multiple logistic regression analysis confirmed that ARDS was associated with female gender (OR 2.384, 95% CI 1.052-5.401, $p=0.037$), higher ISS (OR 0.226, 95% CI 0.140-0.365, $p<0.0001$ for ISS $<$ 15 vs. $\geq$ 25), and shock (SBP $<$ 90 vs $\geq$ 90, OR 1.937, CI 1.183-3.169, $p=0.0086$) at the first point of medical care.

Critical care resource utilization was significant higher in patients with ARDS. Ventilator days (7.1 vs. 3.7 mean days), ICU days (11.2 vs. 5.6 mean days) and hospital length of stay (LOS) (11.0 vs. 5.0 mean days) were significantly increased in the ARDS patient group. Mortality was significantly higher in the ARDS cohort (12.6%) compared to non-ARDS intubated patients (8.8%) and the non-intubated cohort (3.2%).

Multiple logistic regression analysis also confirmed that ARDS was an independent risk factor for death (OR 4.847, 95% CI 2.411-9.743, $p<0.0001$ for ARDS vs. Non-ARDS intubated). Additional independent risk factors for death in this cohort were increased injury severity measured by ISS, decreased SBP reflective of shock state, and decreased admission GCS.

Conclusions: ARDS remains a significant complication in current combat casualty care, and is associated with female gender, higher injury severity and adverse outcomes. ARDS still accounts for death in 0.4% of hospitalized casualties in current military medical care.

FINAL TECHNICAL PROGRESS REPORT
July, 2009

Section I - Recipient and award information:

Title: Acute Lung Injury/Acute Respiratory Distress Syndrome (ALI/ARDS): Risk Factors, Prognostic Factors, Management and Outcome.

Principal Investigator: **Lena M. Napolitano MD, FACS, FCCP, FCCM**
University of Michigan, Ann Arbor, Michigan

Award Reference Number: FA7014-07-C-A010
DRDA Number: 08-0476 (Project Representative Kathryn A. DeWitt, dewitt@umich.edu
Direct Sponsor: Department of the Air Force

Start Date: 1 November 2007
Expected Completion Date: 30 June 2009

Section II - A brief introduction covering the purpose and scope of the project at this stage and its relevance to the overall effort. This should be updated periodically to reflect movement through the life of the project.

Acute respiratory distress syndrome (ARDS) is the sudden, often fatal, acute process by which there is moderate to severe loss of lung function. This occurs following another acute medical condition, such as trauma, pneumonia, sepsis and other etiologies. Each year in the United States there are more than 200,000 cases of acute lung injury (ALI) and ARDS, which are associated with over 75,000 deaths and over 4 million intensive care unit and hospital days of care. The mortality and morbidity rates associated with ALI and ARDS are considerable, with significant impact on public health. The in-hospital mortality rate is very high, with reports ranging from 38.5% to greater than 50%. Most patients who survive ARDS and do not have pre-existing lung disease regain excellent lung function. The challenge is getting them to survive ARDS and its associated severe hypoxemia.

Of particular concern are the reports of combat casualties with severe ARDS in young, otherwise healthy, injured military personnel, some relating to bomb blasts. Setting up systems to provide optimal ALI and ARDS care and management within the Department of Defense, particularly in the far-forward arena and in combat support hospitals, is particularly important to both maintain readiness and force protection, as well as in the continued provision of clinical care during transport and in the provision of definitive care. Research investigation regarding risk factors for ALI and ARDS in the combat setting is also of great importance, since potential efforts to prevent ARDS could be undertaken if these factors are identified. Support of this ARDS research is critical in meeting the needs of military combat casualties. Tested ARDS prevention, prognostic and treatment strategies developed by University of Michigan could ultimately reduce death related to ALI and ARDS, and potentially prevent ALI and ARDS as a complication in injured military personnel.

This Joint Theater Trauma Registry (JTTR) data query seeks to assess the epidemiology and specific risk factors for ARDS in military combat casualties and review current ARDS treatment strategies and outcomes. Specific risk factors that will be investigated include blood transfusion, bomb blast injury, altitude, and patient outcome (survival vs. ALI/ARDS-related death vs. death unrelated to ALI/ARDS).

HYPOTHESES/RESEARCHQUESTIONS:

- What is the epidemiology of ALI/ARDS in combat casualty care in injured military personnel?
- What are the specific risk factors for ALI/ARDS in combat casualty care?
- Is blood transfusion a specific risk factor for ALI/ARDS in combat casualty care?
- Is bomb blast injury or altitude a specific risk factor for ALI/ARDS in combat casualty care?
- What are the current ARDS treatment strategies that are being used in combat casualty care?
- What are the short-term outcomes (ICU & hospital mortality, ICU & hospital length of stay, duration of ventilation, ventilator-free days, organ failure) of patients with ALI/ARDS in combat casualty care?

This Revised Statement of Work (Table below) describes the primary goals of the research for the first year (FY2008 funding). The entire work was initially planned as a 3-year program, ending at the close of FY2010, but only the first year was funded. The primary objectives of this proposal are threefold:

First, to assess the epidemiology and specific risk factors for ALI/ARDS in military combat casualties and review current ARDS treatment strategies and outcomes. Specific risk factors that will be investigated include blood transfusion, altitude, and bomb blast injury.

Second, to develop and implement a comprehensive protocol-driven ALI/ARDS treatment program in combat casualty care.

Third, to support fundamental translational research into the pathophysiology of ALI/ARDS in combat casualties which will aid in the development of innovative and technologically advanced treatment and support strategies for ARDS, early identification of patients at risk for ARDS with biomarkers (systemic and local), and examination of unique aspects of ARDS in combat particularly with regard to bomb blast injuries and the effect of altitude.

During the first year, we plan to assess the epidemiology and specific risk factors for ARDS in military combat casualties and review current ARDS treatment strategies and outcomes in the JTTR. Specific risk factors that will be investigated include blood transfusion, altitude, and bomb blast injury.

Revised Statement of Work

Milestone	Due Date	Acceptance Criteria	% of Effort	Cumulative Effort
Year One (Study One)				
Kickoff Meeting	28 Sep 2007	Completion of meeting	5%	5%
Determine Needed Data Elements	29 Dec 2007	Provided recommended list of elements to AF/SGRS	15%	20%
Statistical Analysis of Initial Data from Query	10 Jun 2008	Provided statistical analysis of initial data from query	5%	25%
Program Management Review	30 Sep 2008	Provided white paper summarizing initial results and issues encountered	20%	45%
ID Risk Factors for ALI/ARDS	30 Dec 2008	Provide report from initial data query	10%	55%
ID Risk Factors for ALI/ARDS	30 Mar 2009	Provide report from second data query	10%	65%
Review ALI/ARDS epidemiology, outcomes , and contribution to fatality	30 Jun 2009	Provide report and submit manuscript for peer-reviewed publication	25%	90%
Final Report	30 Jun 2009	Provide Final report to AF/SGRS	10%	100%

Yellow shading signifies completion of milestone.

Section III – The spreadsheet below provides a brief summary of progress or problems to-date on listed tasks, milestones reached and deliverables completed.

Section III Spreadsheet

Deliverable/Task	Date Project Started	Current Week of Project	Percent Complete	Comments	Date Complete (or est. date) Enter date here	Deliverable Sent to	Date Sent
1: Review Joint Theater Trauma Registry (JTTR) and Data Dictionary to determine necessary data elements for ALI/ARDS and disease-specific outcome variables							
- Submit Military IRB Protocol for Expedited Review of ALI/ARDS study.	Submitted 11-8-2007	--	100%	--	11-8-2007	Thomas C. Jefferson Col, MC Chairman, Privacy Board	11-8-2007
- Obtain Military IRB Approval for JTTR use	11-18-2007	--	100%	Delayed – see below	12-20-2007	Major Jeremy Cannon	12-20-2007
- Obtain Data Dictionary for Review – Version 1 and Version 3	11-8-2007	--	50%	Received Data Dictionary for Version 1 only	--	--	--
- Obtain de-identified JTTR entire dataset from Version 1 and Version 3 to evaluate potential data elements for definition of ALI and ARDS (paO2, FiO2, ventilator information, ventilator variables – PEEP, PIP, etc)	11-18-2007	--	0%	Request for JTTR data submitted immediately on date IRB approval obtained 12-20-2007	--	--	--
Received Data Release from ISR – dated 4-30-2008	11-18-2007	--	100%	Request for Data Release from ISR submitted by Major Cannon	4-30-2008	Major Jeremy Cannon	4-30-2008
2: Review JTTR to determine specific risk factors for ALI/ARDS in combat casualty							
- Univariate analysis to determine specific risk factors for ALI/ARDS	11-18-2007	--	100%	Obtained initial data query results 6-3-2008, 127 patients	6-3-2008	Major Lance Anicelli	6-16-2008, sent in email with attachment “Explore”

- Multivariate analysis to determine specific risk factors for ALI/ARDS		--	N/A	Not possible to perform due to inadequate sample size	--	--	--
- Univariate and multivariate analysis to determine specific risk factors for ALI/ARDS	Data from second data query obtained 11-24-2008	--	100%	Obtained second data query	5-2009	Doug Gibson PhD	May 2009 Monthly report
3: Review JTTR to investigate blood transfusion as a specific risk factor for ALI/ARDS in combat casualty							
- Univariate analysis (PRBCs, FFP, plts, fresh whole blood)	11-18-2007	--	N/A	JTTR review of data source – not reliable data	--	--	--
- Multivariate analysis	Not possible, need new data source	--	N/A	Not possible	--	--	--
4: Review JTTR to investigate Bomb Blast Injury as a specific risk factor for ALI/ARDS in combat casualty, particularly with regard to severity of ARDS							
- Assess prevalence of ALI and ARDS	Data from second data query obtained 11-24-2008	--	100%	Completed	3/2009	Doug Gibson PhD	March 2009 Monthly report
- Determine association of ALI and ARDS with Bomb Blast injury	Data from second data query obtained 11-24-2008	--	100%	Completed	3/2009	Doug Gibson PhD	March 2009 Monthly report
5: Review of ALI/ARDS epidemiology and outcomes in combat casualty using JTTR and additional data sources as necessary							
- Assess prevalence of ALI and ARDS and associated morbidity and mortality	11-18-2007, Second query data obtained 11-24-2008	--	100%	Completed	5/2009	Doug Gibson PhD	May 2009 Monthly report
- Determine severity of ARDS, Severe ARDS defined as P/F ratio < 100	11-18-2007, Second query data obtained 11-24-2008	--	N/A	Unable to complete as data not available in JTTR	--	N/A	N/A
6: Review of all deaths in combat casualty using JTTR and additional data sources as necessary to determine whether ALI/ARDS was a contributing cause							
- Determine overall mortality rate in JTTR	Data from second data query obtained 11-24-2008		100%	Completed	3/2009	Doug Gibson PhD	March 2009 Monthly report
- Determine causes of mortality in JTTR and whether ALI and ARDS were contributing causes	11-18-2007	--	N/A	Not possible to perform, inadequate data source	--	--	--

Also: Copies of all publications, press releases, articles, etc. resulting from the studies above

Date of Status Report:

Form Completed by:

Signature:

Section IV – Supporting information for Section III:

- Possible deviations on deliverables based on inability to obtain JTTR data query.
- Current problems that have impeded performance along with proposed corrective action planned or underway:

- A number of problems that have impeded performance of this contract related to the ability to obtain specific data from the JTTR, but we have also learned a great deal regarding how to use the JTTR for meaningful research:
    - **Obtaining Military IRB approval for use of JTTR.** Required multiple emails and teleconferences after successful submission of the Military IRB protocol on 11-8-2007 by Major Jeremy Cannon. Initially required intervention on the part of Douglas B. Gibson, Ctr, PhD, CIP who initiated contact with Dr. Thomas Jefferson and determined where the protocol was held up 12-20-2007. Protocol was unfortunately left unattended for a prolonged period of time. There was no problem with the submission – it was just not addressed in a timely manner. This resulted in a 3 month delay from the project initiation to IRB approval.
    - **Received Data Dictionary for Version I only** 11-18-2007. No data dictionary for Version 3 provided.
    - **Request for JTTR Data query submitted immediately on date of IRB approval** (12-20-2007)
    - **Awaiting the data query results.** Major Jeremy Cannon submitted the request for the query immediately, and we have asked the query to be performed using ALI or ARDS in the "Complications" field of the JTTR, and will also search by ICD-9 and CPT codes as delineated below.

There are 3 common methods used to detect ARDS: Clinical screening, chart review and diagnostic coding. Since we will be using the JTTR, clinical screening and chart review are not feasible. We can use the American European Consensus Conference definition of ARDS (PaO2/FiO2 ratio less than 200 and noncardiogenic bilateral pulmonary infiltrates) and ALI (PaO2/FiO2 ratio less than 300), but it is not clear if these data are available in the JTTR. ICD-9 codes can be utilized

518.5 includes pulmonary insufficiency following trauma and surgery, ARDS, pulmonary insufficiency following shock, surgery, trauma, shock lung. This code excludes ARDS associated with other conditions (518.82) and pneumonia.

518.82 includes other pulmonary insufficiency, not elsewhere classified, acute respiratory distress, acute respiratory insufficiency, ARDS not elsewhere classified. This code excludes ARDS associated with trauma or surgery (518.85), pumonary insufficiency following trauma or surgery (518.85).

518.81 includes respiratory failure, acute and/or chronic. Excludes: Acute respiratory distress (518.82), respiratory arrest (799.1).

It is not clear whether ICD-9 codes are available in the JTTR. Alternatively, the ICD-9 codes of 518.81, 518.5 and 518.82 can be cross-referenced with the procedural codes for ventilatory support (96.70, 96.71, 96.72). This search may increase the yield of patients with possible ALI and ARDS since coders may not include the codes for ARDS if they do not see if written in the patient progress notes clearly. Furthermore, we know that clinicians underdiagnose ALI and ARDS. An initial query to just pull the number of patients with these codes might be useful. But all other queries must include all the other trauma data elements present in the JTTR as potential risk factors or treatment factors that may impact on the incidence of ALI/ARDS and all-cause outcome.

Alternatively, the initial search can be for all intubated and mechanically ventilated patients in the JTTR, or for all patients with ICD-9 codes 518.5 and 518.82 without additional constraint. The ICD-9 code 518/81 may not be searched because its descriptors do not include ARDS, but there may be errors in coding that should be

considered. The second search can incorporate the same ICD-9 codes (518.5 and 518.82) with the additional mandate of ventilatory support (procedural codes 96.70, 96.71 and 96.72, established in 1991). Some studies have suggested that this combination of ICD-9 disease and procedure codes representing the ICD-9 ARDS criteria mandates that the ARDS patient must meet all of the following criteria:

1. Have a code directly indicated ARDS in the ICD-9 description;
2. Be on concurrent ventilatory support, and
3. Have required >/= 4 days of ventilatory support unless the disease was fatal within that time (lower limit) or have required ventilatory support of unspecified duration, survivors and nonsurvivors (upper limit).

- Despite Military IRB approval from this 12-20-2007 onward, we had been unsuccessful at obtaining data from JTTR
- Multiple emails and teleconferences (with Jeremy Cannon, with Bill Beninati with JTTR personnel and CTR (Combat Trauma Registry) personnel to attempt to obtain data for this research proposal. Ongoing discussion between with Jeremy Cannon and Bill Beninati. Also contacted Michelle (Myung) Park at USAISR for assistance. Continued discussion re who are the correct individuals to provide assistance, Dr. Beninati provided information regarding Dr. Jenkins will be leaving the military and it would be best to consider switching the military PI to Dr. Beninati at this time. Discussion regarding whether we should contact Dr. John Holcomb regarding the feasibility of this request (multiple emails, multiple teleconferences)
- **Received Data Release from ISR – dated 4-20-2008.**
- **Obtained results from initial data query from JTTR on 6-3-2008.** This documented that it took approximately 6 months from the time of IRB approval to the time of initial data receipt.
- **Initial data query:** Only 127 patients were present in this data query retrieved based on ICD-9 codes for acute respiratory failure for the entire time period of the JTTR. This sample size is very small, and significantly underestimates the potential patients with ALI and ARDS.
- I am concerned about a number of issues:
- 1. The total number of patients that the query retrieved is very small over this time frame.
- 2. We are missing a number of data elements on many patients and I cannot tell if it is due to the fact that the data are not in the JTTR or that there was a problem with the way that the data query was performed
- 3. No data was provided regarding the control cohort, i.e. patients that did NOT have acute respiratory failure.
- Teleconference June 16, 2008 with Dr. William Beninati re inability to obtain data from JTTR for this data query and questions above. Dr. Beninanti spoke with Major Annicelli and MaryAnn Spott directly about importance of this data query.
- Teleconference on June 17, 2008 with Major Jeremy Cannon and personnel who performed the data query – Susan West and Michelle Maddin. I again asked why we could not obtain the entire de-identified data from JTTR (with removal of any fields that were confidential data) and therefore have the ability for my statistical team to do the data query here. I again received a response that this was not possible. After significant discussion, it was felt that the only feasible solution was to do a 1-year query (calendar year 2007) to determine the number of patients received in the query results. This was approved by Don Jenkins. This request was not completed.
- I contacted Dr. John Holcomb to request his intervention re obtaining data from JTTR. After speaking with him, he suggested we set up a meeting for July 18, 2008 with Drs. Holcomb, his replacement Dr. Blackbourne, Dr. Brian Eastridge who will assume the responsibility of Director of JTTR from Dr. Jenkins, Susan West, and Jeremy Cannon to represent our research goals. I participated by teleconference. We discussed potential options for data queries and reviewed the difficulties we have had in data access. Dr. Holcomb reviewed data query limitations that we were not aware of.

- We have provided a **recommended list of elements** for the data query, and a data query has been submitted by Jeremy Cannon – we are awaiting the results of this ***second query*** of the JTTR for this ARDS research project.
- 11-24-2008 – We obtained the second query dataset and have initiated the appropriate statistical analyses in order to determine the incidence and prevalence of ARDS and perform the univariate and multivariate analyses to determine risk factors for ARDS in combat casualty care. Frequent meetings with statistician/epidemiologist and research team to review data query results and determine what additional analyses are required. We are considering solutions to some of the issues encountered in the data query results as to how the data is provided, particularly with regard to duplication of patients and information in the dataset as they travel from one site to another, i.e. combat support hospital to Landstuhl.
- **December 2008.** We have completed the initial analysis of the second query dataset. The files were initially imported into SAS for statistical analysis. There are 69 variables in the new dataset vs. 27 variables in the previous dataset. There are 15 possible matches in the two datasets (see attached file – word document). There are 38,218 observations in the dataset. Unfortunately, there are many replicates for each patient subject, and therefore it will take some time to determine how best to avoid duplicity and retain as much information as possible. It is also clear in this second query that the JTTR database changed over time, and there are different data fields, and different methods for capturing that data in the data fields for the different time periods. This will make the statistical analysis particularly challenging.
- **January 2009.** We are in the process of data cleaning and clarification (see attached – Summary_02062009). We have categorized all unique facilities by Level (see attached – uniquefacilitynames 2 – Categorized.xls), clarified the number of unique subjects (n=4666), determined all duplicate files (reduced from 903444 data lines to 311172 after elimination of duplicates), evaluated percent of missing data (see attached report – missingreport.doc), evaluated extent of missing data by injury date (see attached report – missingandinjurydate.pdf), and provided an initial summary of the data, organized as categorical data (categorical summary) and continuous data (continuous summary). We are now in the midst of evaluating all of these data elements to ensure accuracy (need to reconcile "ventilator" and "assistedresp" if these responses are not consistent) before we begin the extensive data analysis for patients with respiratory failure requiring mechanical ventilation, and ALI and ARDS patients.
- **February 2009.** We have completed preliminary statistical analysis of the JTTR data and have submitted an abstract to AAST entitled "Incidence and Mortality of ARDS in Combat Casualty Care" (see below). We have been in contact with Susan West to clarify a number of questions about the data that we received, and are still in the midst of clarifying and cleaning the database. We did identify that there are a number of inconsistencies in the database, i.e. patient listed as "not intubated" but there is data regarding "ventilator days" suggesting that the patient was indeed intubated and mechanically ventilated. The data regarding transfusions and fluid resuscitation is incomplete and we have asked Susan West to determine whether an alternate data source for blood transfusion is available, as Dr. Holcomb had mentioned that previously in one of our teleconferences regarding JTTR data.
- **March 2009**. Abstract accepted for presentation at AAST Annual Meeting September 2009.
- Communication with Philip C. Spinella MD regarding data for blood and blood product transfusion. Ongoing deliberations with Dr. Spinella regarding possible superior or additional data sources for these data since JTTR data is inadequate and not reliable regarding blood product transfusion.
- **April 2009.** Ongoing data analyses to evaluate all other risk factors for ARDS and adverse outcome, univariate and multivariate analyses.
- **May 2009.** Ongoing data analyses to evaluate potential differences in ARDS prevalence and outcomes over time (i.e. early in the conflict vs. later time points, differences in each year of the database)

- Ongoing data analyses to evaluate ICU utilization data for entire cohort and ALI/ARDS cohort.
- Ongoing data analyses to evaluate critical care transport management for entire cohort and ALI/ARDS cohort
- Ongoing data analyses to evaluate risk factors for adverse outcome in patient with ALI and ARDS.

Incidence and Mortality of ARDS in Combat Casualty Care

Park PK, Cannon JW, Ye W, Beninanti W, Blackbourne LH, Eastridge BJ, Holcomb JB, Napolitano LM

Objective: Advances in military medicine and transport have improved coordinated trauma care delivery to the critically injured soldier. In the Vietnam War, approximately 0.4% of hospitalized casualties died from ARDS. We sought to evaluate the current incidence, mortality and resource utilization of ARDS in current combat casualty care.

Methods: The Joint Theater Trauma Registry was queried for US military personnel (excluding non-US, non-military cases) injured between June 8, 2001 and July 17, 2008. The cohort was classified as having 1) ARDS, 2) intubation, without ARDS, or 3) neither. Demographics, trauma variables & outcomes were compared.

Results: The query yielded 4666 individuals with 4700 separate records. 152 ARDS cases (3.2%) were identified; overall mortality was 12.6%. ARDS was associated with female gender and with higher ISS, shock and tachycardia at the first point of medical care. Ventilator days, ICU days and LOS were significantly increased in the ARDS group.

Variable	ARDS	Non-ARDS Intubated	Neither	All
N	152	2213	2335	4700
Age, mean ± SD	26.1 ± 6.0	25.8 ± 6.5	26.4 ± 6.8	26.1 ± 6.6
Gender F, % (n)	5.2 (8) *§	2.2 (47) §	2.6 (63)	2.6 (118)
Blast Injury, % (n)	69.8 (106) §	70.0 (1550) §	58.6 (1370)	64.4 (3026)
GCS 3-8, % (n)	42.6 (60) §	44.8 (907) §	2.4 (40)	25.8 (1007)
ISS05 ≥ 25, % (n)	36.8 (56) *§	27.0 (597) §	2.6 (61)	15.2 (714)
BP ≤ 90 on admit, % (n)	14.6 (22) *§	8.8 (186) §	2.0 (43)	5.6 (251)
HR≥ 90 on admit, % (n)	69.6 (105) *§	61.0 (1306) §	35.6 (806)	48.6 (2217)
Vent days, mean ± SD	7.1 ± 5.7 #	3.7 ± 3.6 #	1.0 ± .2	2.5 ±3.1
ICU days, mean ± SD	11.2 ± 10.1 #	5.6 ± 7.0 #	1.5 ± 1.3	3.7 ± 5.7
LOS, median (range)	11.0 (0-142)#	5.0 (0-1171)#	5.0 (0, 737)	5 (0-1171)
Mortality, % (n)	12.6 (19) §	8.8 (193) §	3.2 (75)	6.2 (287)

*$p < .05$ compared to Non-ARDS, intubated, § $p < 0.05$ compared to Neither by X^2 statistic

#$p < 0.001$ compared to Non-ARDS, intubated by Wilcoxon scores test

Conclusions: ARDS remains a significant complication in current combat casualty care, and is associated with female gender, higher injury severity and adverse outcomes. ARDS still accounts for death in 0.4% of hospitalized casualties in current military medical care.

Section V – Should include:

- Include overall financial profile on the report period and of the program total to-date
- Include the man-hours expended by position for the reporting period and cumulatively during the project
- Include costs that have proper support documentation only
- For a quick comparison, it would be helpful to include a chart in this section to show actual expenditures as compared to budget estimates. If deviation is more than 10%, provide details as needed following the chart.

COST ELEMENTS	THIS MONTH	CUMULATIVE
Total Funds Awarded	N / A	
Personnel		243,575.96
Fringe Benefits		58,448.46
Supplies		17,342.84
Equipment		
Travel		5,682.56
Other Direct Costs		
Subtotal		325,049.82
Indirect Costs		169,149.91
Fee		
Total Expenditures		494,199.73
Award Funds Remaining		16,114.27

Project-related trip reports:

Section VI - A description of work to be performed during the next reporting period:

No further reporting periods. Recommend use of remaining award funds support for obtaining blood product transfusion data to link with ARDS data to evaluate as risk factor for ARDS.

Respectfully Submitted:

Lena M. Napolitano

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